REMARKS

In accordance with the present invention, there are provided genes encoding neuronal nicotinic acetylcholine receptor subunits and proteins encoded thereby. In particular, the invention relates to a family of novel mammalian neuronal nicotinic acetylcholine receptor subunits, for example, the beta2 subunit, which is a non-agonist binding subunit. The invention receptor subunit genes and the protein encoded thereby can be used for a variety of applications, *e.g.*, for drug design and screening. Moreover, the transformed cell lines expressing specific receptor subunits can be produced in quantity for reproducible quantitative analysis of the effects of drugs on receptor functions.

Claims 7, 34, 39 and 42 are amended herein. These amendments do not introduce new matter as they are fully supported throughout the specification and claims as originally filed. Amendments to the claims place the instant application in condition for allowance, or alternatively, place the claims in better form for consideration on appeal. Accordingly, entry of the amendments herein is respectfully requested. Upon entry of the amendments submitted herewith, claims 7 and 34-44 remain pending. A complete set of the claims as they will stand upon entry of the proposed amendments is presented in the Listing of Claims beginning at page 2 of this communication.

A substitute set of drawings is provided herein as Appendix A. The figure numbers of the instant application are amended herein in accordance with the Examiner's objection. Table 1, below, provides a correlation between the numbering of the Figures as originally filed and the numbering of the Figures as presented in the Substitute Set of Drawings submitted herein. In conjunction with the Substitute Set of Drawings, a replacement specification which incorporates the updated figure numbers was previously submitted in Applicant's Response of August 22, 2003.

Table 1

Figure # as originally filed	Figure # in Substitute Set of Drawings
1	1
2A-1	2A
2A-2	2B
2A-3	2C

Figure # as originally filed	Figure # in Substitute Set of Drawings
2B-1	3A
2B-2	3B
2B-3	3C
3A	4A
3B	4B
4A	5A
4B	5B
5A	6A
5B	6B
6A	7A
6B	7B
7A	8
7B-1	9A
7B-2	9B
7B-3	9C
8	10
9A	11A
9B	11B
10A	12A
10B	12B
11	13
12	14
13A	15A
13B	15B
13C	15C
14A	16A
14B	16B
14C	16C
14D	16D
15A	17A

Figure # as originally filed	Figure # in Substitute Set of Drawings
15B	17B
15C-1	18A
15C-2	18B
15C-3	18C
16	19
17A	20A
17B	20B
18A	21A
18B	21B
19A	22A
19B	22B
19C	22C
20	23
21	24
22	25
23	26
24A	27A
24B	27B
24C	27C
25A	28A
25B	28B
25C	28C
26	29
27	30
28	31
29	32

I. Drawings

The objection to the figures as allegedly failing to meet the requirements of 37 C.F.R. §1.84(U)(1), for employing figure numbers such as "7B(1)", has been obviated by the substitute set of figures submitted herein. The updated figure numbers have been incorporated throughout the replacement specification, which was previously submitted in Applicant's Response of August 22, 2003. Reconsideration and withdrawal of this objection are respectfully requested.

II. 35 U.S.C. §112, First Paragraph

A. Claims 7 and 34-44

The rejection of claims 7 and 34-44 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention is respectfully traversed and has been rendered moot by the amendments submitted herewith. Specifically, the Examiner has stated that these claims, drawn to specified amino acid or nucleotide sequences, recite Figures which do not depict any sequences. By the present communication, the Figure numbers have been updated in the Substitute Drawings. Additionally, claims 7, 34, 39 and 42 are amended herein to recite the updated Figure numbers. Therefore, this basis for rejection of claims 7 and 34-44 is moot. Thus, Applicants respectfully request reconsideration and withdrawal of this basis for rejection.

With respect to claim 39 Applicants respectfully disagree with the Examiner's assertion that this claim is allegedly a single means claim. Applicants further disagree with the Examiner's assertion that "because any polynucleotide will hybridize to any other polynucleotide under some set of conditions, the hybridization limitations to the claimed polynucleotide are meaningless" (Official Action, page 3, paragraph 1).

Claim 39, as amended herein, is drawn to a polynucleotide encoding a beta2 subunit of a neuronal acetylcholine receptor, wherein said polynucleotide has at least 15 contiguous bases that hybridize under *high stringency conditions* to the complement of the nucleotide sequence shown in Figures 9A-9C, wherein said beta2 subunit has one or more recited functional properties. Support for the phrase "high stringency conditions" is provided throughout the

specification, such as at page 60 in paragraph [0205] ("the cDNA insert from λHYA5-1 was isolated, radiolabeled and used for **high stringency** screening of 1 x 10^6 plaques..." [emphasis added in bold]), and at page 83 in paragraph [0285] ("one million plaques were screened at **high stringency** using a radiolabeled exon 5 DNA probe..." [emphasis added in bold]).

The term "high stringency" refers to DNA hybridization conditions which are well known to one of ordinary skill in the art. Optimization of high stringency conditions to achieve hybridization with a particular polynucleotide is within the scope of routine experimentation. Provided herein are copies of two Web articles in support of Applicants' assertions, one which illustrates an example of high stringency conditions (Exhibit C: http://www.piercenet.com/Objects/View.cfm?type=Page&ID=F02D8F06-630B-46F7-9022-FA75EBDB9E60) and another article which summarizes optimization of hybridization stringency conditions (Exhibit D: www.roche-applied-science.com/dig/dig_hints04a.htm). The first article provides an example of a representative solution used for high stringency hybridization:

> High stringency wash buffer, 0.5X SSC, 0.1% SDS, or ultrahigh stringency wash, 0.1X SDS, 0.1% SDS may be used if needed. [Citation highlighted within Exhibit C.]

The second article describes routine factors which are varied to achieve hybridization :

> For **any** hybridization, **stringency can be varied** by manipulation of three factors: temperature, salt concentration, and formamide concentration. [Emphasis added in bold; citation highlighted within Exhibit D.]

As evidenced by these two citations in particular, "high stringency" is a term readily understood by one of ordinary skill in the art. Furthermore, a number of factors which are described in the literature, such as temperature and salt concentration, are routinely optimized when the ordinary artisan conducts any hybridization experiment. Moreover, these exemplary articles provide guidance on how to vary these well known factors in order to achieve high stringency in hybridization. For example, the article in Exhibit D provides a table which states that "High temperature increases stringency [whereas] low temperature decreases stringency". Thus, conditions of "high stringency" are well known to one of ordinary skill in the art and optimization of stringency conditions to achieve successful hybridization with a particular probe are within the scope of routine and undue experimentation.

Applicants respectfully disagree with the Examiner's assertion that "because any polynucleotide will hybridize to any other polynucleotide under some set of conditions, the hybridization limitations to the claimed polynucleotide are meaningless" (Official Action, page 3, paragraph 1). Claim 39, as amended herein, recites high stringency conditions for hybridization, and not any arbitrary set of conditions. Thus, the Examiner's assertion that "any polynucleotide will hybridize to any other polynucleotide under **some** set of conditions" (Official Action, page 3, paragraph 1, emphasis added in bold) does not apply to claim 39, which explicitly recites a particular set of hybridization conditions, *i.e.* high stringency. Therefore, Applicants respectfully submit that this basis for rejecting claim 39 has been rebutted and reconsideration and withdrawal are requested.

B. Claim 35

The rejection of claim 35 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention is respectfully traversed and has been rendered moot by the present communication. Specifically, the Examiner has alleged that the specification does not assert "that all restrictions on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent." Applicants submit herein a declaration under 37 C.F.R. § 1.808 (Exhibit B) which states that all restrictions imposed by the depositor on the availability to the public of deposited material will be irrevocably removed upon granting of the patent. Therefore, this rejection of claim 35 is moot. Accordingly, Applicants respectfully request reconsideration and withdrawal of this basis for rejection.

III. 35 U.S.C. §112, Second Paragraph

Applicants respectfully traverse the rejection of claims 7 and 34-44 for allegedly being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

With respect to claims 7 and 34-41, which allegedly lack antecedent basis for reference to "the nucleotide sequence set forth in Figure 9(A), 9(B), and 9(C)" (Official Action at page 5, item 7.1), the rejection has been rendered moot by the Substitute set of drawings submitted herein which has updated Figure numbers. Additionally, claims 7 and 34 are amended herein to

recite the updated Figure numbers. Therefore, this basis for rejection is moot. Accordingly, Applicants respectfully request reconsideration and withdrawal of this basis for rejection.

With respect to claims 42-44, which are allegedly "confusing because the amino acid sequences of the subunits recited therein do not appear in the figures recited therein" (Official Action, page 5, paragraph 4), the rejection has been rendered moot by the Substitute set of drawings submitted herein which has updated Figure numbers. Additionally, claim 42 is amended herein to recite the updated Figure number. Therefore, this basis for rejection is moot and reconsideration and withdrawal are respectfully requested.

With respect to claims 34-44, Applicants respectfully disagree with the Examiner's assertion that these claims are allegedly vague and indefinite for use of the term "beta2." The Examiner cited Paper Number 6, section 7 as the reason of record for the basis of this rejection, which states:

> Because the instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of a "beta2" subunit an artisan can not determine if a compound which meets all of the other limitations of a claim would then be included or excluded from the claimed subject matter by the presence of this limitation. [Official Action of October 22, 2001]

Contrary to the Examiner's assertion, the instant specification provides a clear description of the structure and function of the beta2 subunit. Such description in the specification and the language of the claims define the metes and bounds of the invention.

First, the gene structure, amino acid sequence, and DNA sequence of the beta2 subunit is described by reference to Figures 8, 9A, 9B and 9C. Additionally, various functional properties for characterizing the beta2 subunit are provided in the specification. For instance, beta2 subunit is described in the specification as:

i) being able to substitute for the muscle beta1 subunit in the formation of an acetylcholine receptor, but not being able to substitute for the gamma or delta subunit of a neuronal nicotinic acetylcholine receptor (see page 56, line 3 to page 58, line 3);

ii) not binding acetylcholine, nicotine or analogs thereof (see page 79, line 16 to page 80, line 14);

iii) forming, in conjunction with an alpha3 or an alpha4 subunit, a neuronal nicotinic acetylcholine receptor that is blocked by bungarotoxin 3.1 but not by α-bungarotoxin (see page 26, lines 1-10, and on page 76, line 1 to page 81, line 20); and

iv) forming, in conjunction with an alpha2 subunit, a neuronal nicotinic acetylcholine receptor that is not blocked by either bungarotoxin 3.1 or α-bungarotoxin (see page 26, lines 11-15, and on page 76, line 1 to page 81, line 20).

It is respectfully submitted that the use of functional language, such as the functional properties discussed above, to describe the term "beta2" in claims 34-44 is appropriate and in accordance with the MPEP. Section 2173.05(g), explicitly states that "functional language, does not in an of itself, render a claim improper."

Therefore, contrary to the Examiner's assertion, the instant specification and the language of claims 34-44 provide a clear description of structural and functional properties of beta2 which would be readily understood by one of ordinary skill. Thus, Applicants respectfully request reconsideration and withdrawalof this basis for rejection.

With respect to claims 42-44, which allegedly do not reference one or more specific amino acid sequences, the rejection has been rendered moot. Specifically, the Examiner has stated that subunits alpha2, alpha 3, alpha4, alpha5, beta3, and beta4 do not correspond to specific amino acid sequences. The Substitute set of drawings submitted herein has updated the Figure numbers and claim 42 is amended herein to recite the updated Figure number which contains the corresponding amino acid sequence.

Furthermore, Applicants respectfully disagree with the Examiner's assertion that the specification does not provide properties that are unique to the recited subunits. Claim 42 recites both structural and functional properties for the claimed subunits. For instance, the amino acid sequences for the subunits are provided in the referenced figures and functional properties of the subunits are described in claim 42 and in sections of the specification cited above in Section III(C) of this response. Therefore, Applicants respectfully request reconsideration and withdrawal of this basis for rejection.

CONCLUSION

In view of the above amendments and remarks, the present application is respectfully submitted to be in condition for allowance. Accordingly, reconsideration and favorable action with respect to the pending claims is respectfully requested. In the event any issues remain to be resolved in view of this communication, the Examiner is invited to contact the undersigned at the number given below so that a prompt disposition of this application can be achieved.

Respectfully submitted,

Date: March 15, 2004

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ENCLOSURES:
Exhibit A- Substitute Set of Drawings

Exhibit B- Declaration under 37 C.F.R. § 1.808

Exhibit C- http://www.piercenet.com/Objects/View.cfm?type=Page&ID=F02D8F06-630B-46F7-9022-FA75EBDB9E60)

Exhibit D: www.roche-applied-science.com/dig/dig_hints04a.htm